

1.0 AMENDMENT

1.1 IN THE CLAIMS:

Please amend claims 2, 4, 5, and 8, so that the amended text reads as follows:

1. (Original) A ribozyme that specifically cleaves an mRNA encoding a polypeptide that causes or contributes to the disease, disorder, or dysfunction of a cell or a tissue of a mammalian eye.
2. (Currently Amended) The ribozyme of claim 1, wherein said ribozyme specifically cleaves an mRNA encoding a polypeptide selected from the group consisting of rod opsin, RP1, RDS/Peripherin, iNOS, A_{2B} receptor, IGF-1 receptor, alpha 1, alpha 3, and alpha V.
3. (Original) The ribozyme of claim 2, wherein said ribozyme (a) comprises the sequence of any one of SEQ ID NO:2, or SEQ ID NO:90 to SEQ ID NO:105, or (b) specifically cleaves an mRNA comprising a sequence selected from any one of SEQ ID NO:1, or SEQ ID NO:3 to SEQ ID NO:89.
4. (Currently Amended) The ribozyme of claim 3, wherein said ribozyme comprises a sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and SEQ ID NO:105.

5. (Currently Amended) The ribozyme of claim 2, wherein said ribozyme specifically cleaves an mRNA encoding a polypeptide selected from the group consisting of a mutant rod opsin polypeptide, a mutant RP1 polypeptide, a mutant RDS/Peripherin polypeptide, a mutant iNOS polypeptide, a mutant A_{2B} receptor polypeptide, a mutant IGF-1 receptor polypeptide, a mutant alpha 1 polypeptide, a mutant alpha 3 polypeptide, and a mutant alpha V polypeptide.
6. (Original) The ribozyme of claim 5, wherein said ribozyme specifically cleaves an mRNA encoding a mutant rod opsin polypeptide.
7. (Original) The ribozyme of claim 6, wherein said ribozyme specifically cleaves an mRNA encoding a mutant rod opsin polypeptide that comprises a mutation selected from the group consisting of P23H, P23L, Q28H, F45L, L46R, G51A, G51G, G51R, G51V, P53R, T58R, Q64stop, 68-71, V87D, G90D, G106W, C110Y, G114D, R135G, R135L, R135P, P171L, P171S, Y178C, P180A, C187Y, G188R, D190G, D190Y, M207R, H211R, H211P, F220C, C264X, P267L, F220C, C222R, A292E, Q344stop, and P347S.
8. (Currently Amended) The ribozyme of claim 7, wherein said ribozyme specifically cleaves an mRNA that comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID

NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, ~~and~~ SEQ ID NO:63, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, and SEQ ID NO:91.

9. (Original) The ribozyme of claim 5, wherein said ribozyme specifically cleaves an mRNA encoding a mutant RP1 polypeptide, or an A_{2B} receptor polypeptide.
10. (Original) The ribozyme of claim 9, wherein said ribozyme specifically cleaves an mRNA comprising the sequence of SEQ ID NO:64 or SEQ ID NO:1.
11. (Original) The ribozyme of claim 5, wherein said ribozyme specifically cleaves an mRNA encoding a mutant RDS/Peripherin polypeptide.
12. (Original) The ribozyme of claim 11, wherein said ribozyme specifically cleaves an mRNA encoding a mutant RDS/Peripherin polypeptide that comprises a mutation selected from the group consisting of C118, R172Q, R172W, P210R, C214S, P216L, and P219.
13. (Original) The ribozyme of claim 12, wherein said ribozyme specifically cleaves an mRNA that comprises a sequence selected from the group consisting of SEQ ID

NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, and SEQ ID NO:77.

14. (Original) The ribozyme of claim 1, wherein said molecule is a hammerhead ribozyme.
15. (Original) The ribozyme of claim 1, wherein said molecule is a hairpin ribozyme.
16. (Original) A vector comprising a polynucleotide encoding the ribozyme of claim 1, said polynucleotide operably linked to at least a first promoter element that directs expression of said polynucleotide in a mammalian cell.
17. (Original) The vector of claim 16, wherein said vector is a viral vector.
18. (Original) The vector of claim 17, wherein said viral vector is an adeno-associated viral vector.
19. (Original) The vector of claim 16, wherein said promoter element directs expression of said polynucleotide in a retinal cell.
20. (Original) The vector of claim 16, wherein said promoter element directs expression of said polynucleotide in a photoreceptor cell.
21. (Original) The vector of claim 16, wherein said promoter element directs expression of said polynucleotide in a rod or a cone cell.

22. (Original) The vector of claim 16, wherein said promoter element directs expression of said polynucleotide in a Mueller cell, or a retinal pigment epithelium cell.
23. (Original) The vector of claim 16, wherein said promoter element comprises a mammalian rod opsin promoter element.
24. (Original) The vector of claim 16, wherein said promoter element comprises a constitutive or an inducible promoter element.
25. (Original) A virus comprising the ribozyme of claim 1, or a polynucleotide that encodes the ribozyme of claim 1.
26. (Original) The virus of claim 25, wherein said virus is an adenovirus or an adeno-associated virus
27. (Original) An adeno-associated viral vector comprising the ribozyme of claim 1, or a polynucleotide that encodes the ribozyme of claim 1.
28. (Original) The adeno-associated viral vector of claim 27, wherein said polynucleotide is operably linked to at least a first regulatory element that directs expression of said polynucleotide in a mammalian cell.

29. (Original) The adeno-associated viral vector of claim 28, wherein said regulatory element comprises a promoter that expresses said polynucleotide in a cell of a human eye.
30. (Original) A host cell that comprises:
- (a) the ribozyme of claim 1;
 - (b) the vector of claim 16;
 - (c) the virus of claim 25; or
 - (d) the adeno-associated viral vector of claim 27.
31. (Original) The host cell of claim 30, wherein said cell is a mammalian host cell.
32. (Original) The host cell of claim 31, wherein said mammalian host cell is a human cell.
33. (Original) The host cell of claim 32, wherein said human cell is a retinal cell.
34. (Original) The host cell of claim 33, wherein said retinal cell is a photoreceptor cell.
35. (Original) The host cell of claim 34, wherein said retinal cell is a photoreceptor rod or cone cell.
36. (Original) A composition comprising:
- (a) the ribozyme of claim 1;
 - (b) the vector of claim 16;
 - (c) the virus of claim 25; or

- (d) the adeno-associated viral vector of claim 27.
37. (Original) The composition of claim 36, further comprising a pharmaceutical excipient.
38. (Original) The composition of claim 37, wherein said pharmaceutical excipient is suitable for ocular or subretinal administration to a mammalian eye.
39. (Original) The composition of claim 36, further comprising a lipid, a liposome, a nanoparticle, or a microsphere.
40. (Original) A kit comprising:
- (a) (i) the ribozyme of claim 1;
 - (ii) the vector of claim 16;
 - (iii) the virus of claim 25; or
 - (iv) the adeno-associated viral vector of claim 27; and
 - (b) instructions for using said kit.
41. (Original) A kit comprising the composition of claim 36, and instructions for using said kit.
42. (Original) The kit of claim 41, further comprising device for delivering said composition to the eye, retina, or subretinal space of a mammal.
43. (Original) A method for decreasing the amount of mRNA encoding a selected polypeptide in a retinal cell of a mammalian eye, comprising providing to said eye an

amount of the composition of claim 36, and for a time effective to specifically cleave said mRNA in said cell, and thereby decrease the amount of mRNA in said cell.

44. (Original) The method of claim 43, wherein said ribozyme specifically cleaves an mRNA encoding a polypeptide that causes a pathological condition in, or contributes to a disease, disorder, or dysfunction in a cell or a tissue of a mammalian eye.
45. (Original) The method of claim 43, wherein said composition is provided to said eye by direct administration, ocular injection, retinal injection, or subretinal injection.
46. (Original) The method of claim 44, wherein said pathological condition is selected from the group consisting of retinal degeneration, retinitis, macular degeneration, or retinopathy.
47. (Original) The method of claim 46, wherein said retinitis is retinitis pigmentosa.
48. (Original) The method of claim 46, wherein said pathological condition is autosomal dominant retinitis pigmentosa or autosomal recessive retinitis pigmentosa.
49. (Original) The method of claim 46, wherein said pathological condition is macular degeneration.
50. (Original) The method of claim 49, wherein said pathological condition is age-related macular degeneration.

51. (Original) The method of claim 46, wherein said pathological condition is retinopathy.
52. (Original) The method of claim 51, wherein said pathological condition is diabetic retinopathy.
53. (Original) A method for decreasing the amount of a selected polypeptide in a cell or tissue of a mammalian eye, comprising providing to said eye an amount of the ribozyme of claim 1 and for a time effective to specifically decrease the amount of said selected polypeptide in said cell or said tissue.
54. (Original) A method for decreasing the amount of a selected polypeptide in the eye of a mammal suspected of having a pathological condition selected from the group consisting of retinal degeneration, retinitis, macular degeneration, and retinopathy, comprising directly administering to said eye: (a) the ribozyme of claim 1, (b) the vector of claim 16, (c) the virus of claim 25, or (d) the adeno-associated viral vector of claim 27, in an amount and for a time effective to specifically cleave an mRNA encoding said selected polypeptide, and thereby decreasing the amount of said polypeptide in said eye.
55. (Original) A method for treating, decreasing the severity, or ameliorating the symptoms of a pathological condition that results from the expression of at least a first selected polypeptide in a cell or a tissue of a human eye, said method comprising directly administering to said eye: (a) the ribozyme of claim 1, (b) the vector of claim 16, (c) the virus of claim 25, or (d) the adeno-associated viral vector of claim 27, in an

amount and for a time effective to treat, decrease the severity, or ameliorate the symptoms of said pathological condition.

56. (Original) The method of claim 55, wherein said symptoms are selected from the group consisting of atrophic lesions of the eye, pigmented lesions of the eye, blindness, a reduction in central vision, a reduction in peripheral vision, and a reduction in total vision.
57. (Original) A method for decreasing the progression of a degenerative pathological condition of a mammalian eye, comprising providing to said eye: (a) the ribozyme of claim 1, (b) the vector of claim 16, (c) the virus of claim 25, or (d) the adeno-associated viral vector of claim 27, in an amount and for a time effective to decrease the progression of said degenerative pathological condition.